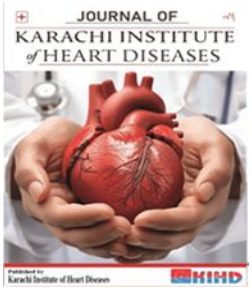

CHANGES IN THE SERIES OF N-TERMINAL PRO-B-TYPE NATRI-URETIC PEPTIDE LEVEL AND HEART FAILURE-RELATED READMISSION

Junaid Mahmood Alam[1], Syed Riaz Mahmood[2]
Department of Clinical Biochemistry lab services and Chemical Pathology, Liaquat National Hospital and Medical College, Karachi-Pakistan[1]
Department of Pathology, Lyari General Hospital, Karachi[2]

ABSTRACT:

Background N-terminal pro–B-type natriuretic peptide (NT-proBNP) is a well-recognized biomarker of cardiac wall stress and a strong predictor of adverse cardiac outcomes in patients with HF. Previous studies from community and hospital-based settings have demonstrated its prognostic value not only for cardiovascular events but also in term of mortality. However, limited evidence exists on the association between changes in NT-proBNP levels and the risk of HF readmission among adult outpatients.

Methods: A retrospective cohort study was conducted on 560 out-patients adult aged ≥30 years had done NT-proBNP measured at two separate visits. Clinical and laboratory data were collected from medical records, and patients were followed for HF readmission events. Logistic regression was used to evaluate associations between NT-proBNP and the risk of readmission; model was adjusted for age, sex, blood pressure, diabetes, renal function, and other cardiovascular risk factors.

Results: A follow up was conducted retrospectively using medical record data over a median follow-up within 6 months, patients with persistently elevated NT-proBNP or those whose NT-proBNP increased between two visits had a significantly higher risk of HF readmission compared with those whose levels remained low. Even in adjusted model, frequently high NT-proBNP was associated with a greater risk of readmission.

Conclusions: In this retrospective outpatient cohort, elevated or rising NT-proBNP levels were independently associated with higher risk of HF readmission. Serial NT-proBNP measurement may serve as a practical tool for identifying high-risk patients who may benefit from close monitoring and preventive strategies

Keywords: Blood Pressure, ischemic heart disease, acute cardiac events

Submitted: 22-01-2026, Revised: 22-02-2026, Accepted:03-03-2026

INTRODUCTION

Heart failure (HF) remains a major public health challenge from many years, which affect over 64 million people worldwide and contributing in substantial outcomes including morbidity, mortality, and healthcare expenditure.[1] Hospital readmission following an index HF hospitalization is recognized as an indicator of disease progression, management, and risk stratification at the time of discharge.[2] This emphasizes the clinical importance of identifying strong predictive markers that could promptly detect patients at high risk for adverse outcomes, including re-hospitalization. HF defined as a clinical condition consequently occur due to structural and/or functional cardiac irregularities, leading to impaired ventricular filling or ejection, often accompanied by elevated natriuretic peptides or evidence of pulmonary or systemic congestion.[3] Although therapeutic treatment has been advanced, but HF persistently cause recurrent hospital readmissions and poor long-term outcome and prognosis, which accentuate the need of improving risk stratification and monitor strategies.[4] In order to confirm HF, biomarkers are essential. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is one of the most extensively validated biomarkers of myocardial stress and cardiac dysfunction among the many biomarkers currently used in clinical practice.[5] Ventricular myocytes release this peptide in response to increased intra-cardiac pressures, wall tension, and volume overload. Because NT-proBNP has a longer half-life and is more stable than the active BNP peptide, it functions as a stable marker. [2, 6] It is essential for the diagnosis, prognosis, and treatment of heart failure in both inpatient and outpatient settings allow for accurate measurement during hospital follow-up as well as at initial presentation.[7] In many HF populations, elevated NT proBNP has been shown to be a prognostic indicator for mortality, readmission, and major

adverse cardiac events as well as a diagnostic marker to differentiate HF from other causes and symptoms.[8]

The predictive value of serial NT-proBNP measurement has been highlighted in recent studies; longitudinal changes in NT-proBNP levels offer a more accurate representation of cardiovascular risk and treatment response than a single baseline value.[9,10] Because a single inconsistent reading may be caused by variations in the clinical characteristics of the patient, such as age and renal function, as well as the dynamic nature of cardiac stress that cannot be fully captured by a single biomarker assessment. Evidence suggests that isolated NT-proBNP values at the time of hospital admission may have limited utility in predicting future readmissions unless incorporated into additional clinical variables or serial assessments that reflect temporal changes in cardiac status. [2, 9] In particular, Journal of American College of Cardiology Heart Failure 2023 demonstrated that repeated NT-proBNP measurements predicted outcomes more accurately than a single test in patients with reduced ejection fraction.[9] Similarly, Circulation reported in 2024 from the ARIC study that elevated NT-proBNP was associated with long-term changes in cardiac structure and function, among older adults even without established HF. [10]

NT-proBNP series measurements and changes over time have drawn attention as potentially better prognostic tools because they enable close monitoring of the patient's biological response to treatment and changes in haemodynamic status. Compared to baseline NT-proBNP alone, repeated NT-proBNP assessments have shown stronger associations with subsequent hospitalizations and mortality in longitudinal analyses of chronic HF retrospective cohorts. Increases in NT-proBNP over time have been linked to an increased risk of HF-related hospitalization or death, and they frequently occur weeks before clinical decompensation.[9] Furthermore, NT-proBNP variations have been linked to outcomes, according to trial analyses; patients who exhibit significant decreases in NT-proBNP during treatment experience fewer cardiovascular events than those who do not..[11, 12] NT-proBNP has been thoroughly investigated as a predictor of cardiovascular mortality [4, 5], but its role in predicting HF-related re-hospitalization, a clinically significant outcome that directly reflects disease progression and healthcare utilization has received less attention. Future studies are still required to determine the relationship between longitudinal changes in NT-proBNP and particular outcomes, such as readmission related to heart failure. Knowing how NT-proBNP varies between two visits in relation to readmission risk may help identify high-risk patients earlier and provide more individualized outpatient care management. This retrospective study aimed to investigate whether temporal changes in NT-proBNP levels, measured across two outpatient visits, are associated with the risk of HF readmission in adults because a significant gap exists in systematically evaluation that whether changes in NT-proBNP could serve as an early warning for readmission risk. Because serial NT-proBNP may have an impact on the adjustment of post-discharge management and follow-up intensity, possibly preventing recurrent hospitalizations and improving patient outcomes, this evidence gap has significant clinical implications. Furthermore, knowing how NT proBNP changes over time correlate with readmissions related to heart failure may improve risk stratification models, guide individualized treatment plans, and help manage heart failure with the best use of available resources.

METHODS

Study Design and Setting

A retrospective cohort study has been done at the Karachi Institute of Heart Diseases, in between January 2023 to December 2023.

Study Population

Adult patients aged ≥30 years with a clinical diagnosis of chronic HF who attended the outpatient cardiology clinic during the study period were screened for availability of at least two NT-proBNP measurements obtained within 6 months during routine follow-up visits, diagnosis of HF with mildly reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF) according to 2021 European Society of Cardiology (ESC) guidelines. [2, 3] On the other hand, recent acute coronary syndrome (ACS) or decompensate HF (<3 months before baseline); severe chronic kidney disease estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m²); active malignancy or severe liver disease; and missing essential clinical or laboratory data were omitted from the present study. After exclusions, 560 subjects were included in the final sample.

Data Collection Procedures

Data was retrieved from the patient's previous record using a standardized form. Two investigators independently verified all entries. Baseline characteristics included: socio-demographics**:** age, gender, and body mass index (BMI); Clinical parameters: systolic and diastolic blood pressure(SBP/DBP), smoking, New York Heart Association (NYHA) class, comorbidities (hypertension(HTN), diabetes mellitus(DM), coronary artery disease(CAD); Laboratory data include NT-proBNP, fasting glucose, serum creatinine, eGFR, total cholesterol, triglycerides(TGs), and low-density lipoprotein cholesterol (LDL-C); Echocardiography: left ventricular ejection fraction (LVEF) and left atrial size; Medications: use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta-blockers, diuretics, and statins.[5-7] Height and weight were measured by using stadio-meter and BMI calculated through standardized formula kg/m2. HTN defined as a mean SBP ≥140 mm Hg, mean DBP ≥90 mm Hg, or self-reported history. Similarly, DM defined as a hemoglobin A1C ≥6.5% or self -reported history. Hypercholesterolemia defined as ≥240 mg/dL total cholesterol or self- reported use of lipid-lowering medication. History of CVD (congestive heart failure, coronary heart disease, angina, heart attack, or stroke) diagnosed by a health care provider. Chronic kidney disease was defined as reduced eGFR.

Outcome Definition

The primary outcome was HF readmission, defined as the first hospitalization due to worsening HF symptoms confirmed by a cardiologist and supported by objective findings such as pulmonary congestion, elevated natriuretic peptides, or echocardiographic evidence.[13]

Outcome Definition

The primary outcome was HF readmission, defined as the first hospitalization due to worsening HF symptoms confirmed by a cardiologist and supported by objective findings such as pulmonary congestion, elevated natriuretic peptides, or echocardiographic evidence.[13]

Ethical Considerations

Current study was approved by the Institutional Review Board (IRB) of Karachi Institute of Heart Diseases. Informed consent was waived due to retrospective nature of the study and the anonymous use of data.

Statistical Analysis

Continuous variables were tested for normality distribution using the Shapiro-Wilk test. The paired t-test was used to compare continuous variables between Visits 1 and 2, with each variable being presented as mean ± standard deviation (SD). The median and interquartile ranges (IQR) are used to express continuous variables that are not normally distributed. In contrast, categorical variables are displayed as percentages and frequencies.

Baseline clinical characteristics of the 560 outpatients were summarized at Visit 1 and Visit 2, and within-patient changes in clinical and laboratory variables. Changes in NT-proBNP between Visit 1 and Visit 2 were categorized into four groups:≤125,125-300, 301-900 and ≥900. HF related readmission rates were compared across these NT-proBNP change groups.

To evaluate the independent association between changes in NT-proBNP and HF readmission, multivariable regression models were constructed. Odds ratio (OR) with 95% confidence intervals (CIs) were reported. All statistical analyses performed on IBM SPSS Statistics version 29.0 (IBM Corp, Armonk, NY), with $p< 0.05$ considered statistically significant.

RESULTS

Table I: Baseline Characteristics of 560 outpatients according to visit 1 and visit 2

Characteristic	Visit 1 (n= 560)	%	Visit 2 (n=560)	%
Age yrs (Mean ± SD)	58.7 ± 11.2		59.8 ± 11.3	
Men No. (%)	298	53.2%	298	53.2%
Women No. (%)	262	46.8%	262	46.8%
HTN No. (%)	230	41.1%	252	45.0%
On antihypertensive medicine	210	37.5%	226	40.4%
Systolic BP, mm Hg (Mean ± SD)	131.4 ± 15.2		129.8 ± 14.6	
Diastolic BP, mmHg (Mean ± SD)	78.6 ± 9.4		77.9 ± 8.9	
LDL	119.3 ± 34.1		116.8 ± 33.2	
TGs	156.8 ± 70.1		151.4 ± 67.8	
On lipid lowering medicine No. (%)	122	21.8%	148	26.4%
DM No. (%)	172	30.7%	188	33.6%
Fasting glucose	122.5 ± 29.8		124.3 ± 28.9	
BMI	23.3 ± 3.8		22.0 ± 3.7	
eGFR	83.6 ± 13.9		82.4 ± 13.7	
Smoker No. (%)	74	13.2%	66	11.8%
NT-pro-BNP, pg/mL (median [IQR])	185 (90-420)		260 (120–570	

Table 1 showed participants were divided into two groups based on the changes occurred in between the two visits in term of percentage and number. Categorical variable defined as in number and percentage in contrary numerical data analyzed through number and standard deviation.

Table 2. Differences in Clinical variables at Visit 1 and Visit 2

Characteristic	Visit 1 (n = 560)	Visit 2 (n = 560)	P Value
Age, y (Mean ± SD)	58.7 ± 11.2	59.8 ± 11.3	0.002
Women (%)	298 (53.2)	298 (53.2)	-
Men (%)	262 (46.8)	262 (46.8)	-
Hypertension (%)	230 (41.1)	252 (45.0)	0.04
On antihypertensive Medication (%)	210 (37.5)	226 (40.4)	0.16
Systolic BP, mm Hg (Mean ± SD)	131.4 ± 15.2	129.8 ± 14.6	0.08
Diastolic BP, mm Hg (Mean ± SD)	78.6 ± 9.4	77.9 ± 8.9	0.22
LDL-C, mg/dL (Mean ± SD)	119.3 ± 34.1	116.8 ± 33.2	0.12
Triglycerides, mg/dL (Mean ± SD)	152.6 ± 70.1	148.4 ± 67.8	0.07
On lipid-lowering medication, No. (%)	122 (21.8)	148 (26.4)	0.03
Diabetes, No. (%)	155 (27.7)	172 (30.7)	0.045
Fastingglucose, mg/dL (Mean ± SD)	119.4 ± 30.2	121.8 ± 29.7	0.08
Body mass index, kg/m² (Mean ± SD)	26.1 ± 3.9	25.8 ± 3.8	0.07
eGFR, mL/min/1.73 m² (Mean ± SD)	83.6 ± 13.9	82.4 ± 13.7	0.07
Current smoking, No. (%)	74 (13.2)	66 (11.8)	0.39
NT-proBNP, pg/mL (median [IQR])	185 (90–420)	260 (120–570	<0.001

The demographic and clinical characteristics of the 560 patients who were enrolled from the outpatient department during both visits were compared and summarised in Table 2. The time between two visits is reflected in the participants' slightly higher mean age, which went from 58.7 ± 11.2 to 59.8 ± 11.3 years. 53.2% of the participants were female, making up more than half

of the cohort. Comparing the two visits, the incidence of HTN rose from 41.1% to 45.

Table 3: Multivariable Regression between HF Readmission with NT- pro BNP level changes

NT-pro-BNP	Visit 1 Patients n (%)	Visit 2 Patients n (%)	Readmission	Odds Ratio (OR)	95% CI	P value
<125	205 (36.6)	230 (41.1)	03 (1.7)	1	-	-
125-300	150 (26.8)	135 (24.1)	04 (11.1)	2.35	1.6-5.2	<0.001
301-900	125 (22.3)	110 (19.6)	07 (13.6)	5.1	3.0-9.7	<0.001
>900	80 (14.3)	85 (15.2)	09 (32.9)	8.4	4.4-15.1	0.000

Adjusted model: *Age, sex, BMI, Systolic blood pressure, diabetes mellitus, HTN, LDL-C, eGFR, smoking status, prevalent CHD*

In multivariable regression, slight or higher increases in NT-proBNP were independently associated with significantly higher risk of 90-day HF readmission. Specifically, patients with > or equal to 900 level had 8.4-fold increase risk of readmission compared with patients achieving < 125 NT pro BNP level. The multivariable model was adjusted for Age, sex, BMI, Systolic blood pressure, diabetes mellitus, HTN, LDL-C, eGFR, smoking status to control for potential confounders. After adjustment it has been identified that patients with rising NT-proBNP between visit 1 and visit 2 had a significantly higher rate of HF readmission compared to the reference group.

DISCUSSION

The present study investigated the association between changes in NT-proBNP levels and HF readmission among outpatients. This study is one of the few from South Asia to examine dynamic changes in the two sets of NT-proBNP rather than single measurements. The principal findings demonstrated that, outpatients exhibited worse cardio-metabolic profiles, those NT-proBNP significantly increased levels between two visits and a more than or equal to quarter rose in NT-proBNP was also strongly and independently associated with HF readmission. These findings provide similar evidence confirmed from previous study that NT-proBNP changing level is an important prognostic biomarker in outpatient cardiovascular management. Current study results were consistent with previous studies specified the predictive power of NT-proBNP in the prognosis of HF.[14] Importantly, serial measurement of NT-proBNP offers greater prognostic accuracy than a single baseline value.[15] A recent meta-analysis reported that repeated NT-proBNP monitoring significantly associated with prediction of re-hospitalization and mortality compared with single measurements.[2]

Furthermore, recent research indicates that it is important to monitor changes in NT-proBNP rather than depending solely on single time point values. Extensive research demonstrates that repeated pro-BNP measurements offer more information for prognosis and can identify risk patterns that cannot be identified by a single reading alone. The observation of a series of NT Pro-BNP readings in outpatients with heart failure and a reduced ejection fraction in the GUIDE-IT study highlighted that elevated NT Pro-BNP levels predict clinical outcomes like hospitalisation or death from cardiovascular events prior to a few weeks, suggesting that elevated NT-proBNP levels are an early biological indicator of impending clinical deterioration. As a result, a sequence of readings rather than a single baseline value guides serious clinical outcomes.[9] Constantly elevated NT-proBNP levels directs neurohormonal activation and subclinical fluid overload which is not directly linked as a symptom but nevertheless has weightage of prognosis.[16] Clinical relevance of serial biomarker monitoring highlights through strong, independent evidence based relationship between increase NT-proBNP and HF readmission. As our study indicated that each more or equal increase in quarter percent NT-proBNP was associated with a nearly threefold increase risk for HF readmission, even after adjusting for age, sex, BMI, DM, renal function, and blood pressure.

These results imply that NT-proBNP may function as a decompensated heart failure early warning indicator. The NT-ProBNP marker's trend series provides the clinician with information about the patient's increasing risk profile. While its levels can dictate the length of time and dosage of medical therapy, this evidence supports the idea that NT-ProBNP guided cardiac management.[16] Another study aligns with data from the GUIDE-IT trial, which showed that dynamic changes in NT-proBNP during follow-up were strongly associated with future HF hospitalizations, even after adjusting for different clinical variables.[17] These findings could be directly implicated among outpatient care in Pakistan and similar lower- and middle-income countries. NT-proBNP testing is relatively affordable, minimally invasive, and easily accessible, all facts make it a feasible tool for outpatient monitoring.

Present retrospective cohort participants had elevated NT-proBNP, were older, had a higher prevalence of DM and HTN, and demonstrated slightly reduced kidney function. Similar to retrospective study done in Romania found that HF with higher NT proBNP level tends to have higher prevalence of DM and worse renal function.[1]Although modest progresses found in readings of blood pressure and lipid levels in between both visits, but NT-proBNP continued to rise, suggesting ongoing subclinical myocardial stress or diastolic dysfunction.

Mean BMI of this retrospective cohort's was almost near normal limits and higher prevalence of DM reflected previous evidence based risk pattern suggested that cardio-metabolic risk occur at younger ages and lower BMI levels among South Asian populations, as compared to Western population.[18]

Despite many evidences there is still a lack for standardized pathway for serial NT-ProBNP and remains confined in many guidelines and clinical setups due to variability in measurement intervals, highest values for clinical action and characteristics of

the admitted patients which influence levels of NT-ProBNP such as age, renal condition or arterial fibrillation.[2]

Incorporating serial NT-proBNP assessments into follow-up visits could guide for prompt intervention such as optimization of diuretic therapy, patient's medication adherence counseling, or early referral for echocardiography for potentially preventing HF related readmissions. European Society of Cardiology 2023 HF guidelines emphasize the importance of natriuretic peptide monitoring for risk stratification and management of HF.[19] Future prospective cohorts with long-term follow-up should be conducted to investigate the best timing and frequency of NT-proBNP monitoring and to assess the significance of any changes that might lead to an intervention. Prognostic accuracy may be increased by including serial NT-proBNP in imaging marker prediction models for left atrial strain, E/e' ratio, and other biomarkers like high-sensitivity troponin and ST2. Furthermore, the establishment of population-based NT-proBNP cutoffs requires region-specific research, particularly from South Asia. Moreover, the growing literature emphasized that dynamic NT-proBNP assessment is more than a research tool, it represents a practical, biologically grounded approach to improving prognostic criteria and directing care protocol in chronic HF. Continuous input is required to align the measurement practices and define actionable thresholds will be essential to realize its full clinical potential.[2, 16]

STRENGTH OF THE STUDIES

This study has numerous significant strengths; it has included a comparatively huge number of outpatient cohort participants, which enhanced the precision of estimation. NT-proBNP was not depended on a single baseline value rather than it was measured at two separate visits, which can strongly have allowed the estimation of longitudinal changes. This method offers a more clinically meaningful analysis of risk factors associated with cardiovascular disease. The use of standardised methods for data collection and statistical adjustment for significant confounders, including age, sex, BMI, diabetes, renal function, and blood pressure, improved the validity of associations. This was another strength. The results of our study also added the important regional-based evidence that may improve global generalizability, as Pakistan is part of the South Asian population, which is frequently under-represented in biomarker research despite having a high burden of cardio-metabolic disease.

LIMITATIONS

Although this study had several strengths but we found some limitations as well. First of all, the study design we used in this study was retrospective observational design which is not suitable for conclusive causal inference. Although the statistical analysis was adjusted for key confounders, unmeasured variables for e.g., medication adherence, socioeconomic status may have influenced the results of study. Furthermore age, renal function, and body composition can be affect NT-proBNP so residual bias cannot be excluded.[3] The sample of current study was drawn from a single tertiary center which limit the generalizability to broader community settings. Finally, we only focused on readmission rather than all-cause mortality; future research should be evaluated both outcomes together to evaluate the complete prognostic influence of series of NT-proBNP changes.

CONCLUSION

In conclusion, this study demonstrated that an evaluating series of NT-proBNP levels has been shown a powerful predictor of HF related readmission among outpatients which is independent of cardio-metabolic risk factors. Series of NT-proBNP assessment may offer a simple, accessible, and effective strategy to diagnose individuals with high risk and prompt management may improve long-term outcomes. Incorporation of assessing series of this biomarker into routine cardiovascular care, particularly in regions with high cardio-metabolic burden will help in prompt management.

.

Conflict of interest

Authors declare no conflict of interest.

REFERENCES

1. Savarese, G. and Lund, L. H. (2017) Global public health burden of heart failure. *Card. Fail. Rev*. 3, 7-11.
2. Arshad, H. S,, Laraib, F., Nikeeta, F., Vandina, F., Gurya, A. A., Farooq, U., Ali, S., Nisar, L., Zamir, M. H., and Akbar, F. (2025) Prognostic Utility of N-terminal Pro-B-type Natriuretic Peptide (NT-proBNP) for Predicting Hospital Readmissions in Patients With Heart Failure: A Systematic Review of Clinical Evidence. *Cureus*. 17, 85242-85249.
3. Bozkurt, B, Coats, A. J. S., Tsutsui, H., Abdelhamid, M., Adamopoulos, S., Albert, N., *et al*. (2021) Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur. J. Heart Fail*. 23, 352-380.
4. Udell, J. A., Bahit, M. C., Campbell, P., Butler, J., Chopra, V. K., Bayes-Genis, A., Bozkurt, B., Petrie, M. C. and Vaduganathan, M. (2025) Prevention of heart failure after acute myocardial infarction. *The Lancet.* 406, 1154-1170.
5. Maisel, A. S. and Daniels, L. B. (2012) Breathing not properly 10 years later: what we have learned and what we still need to learn. *J. Am. Coll. Cardiol*. 60, 277-282.
6. Szumańska, M. (2008) Levels of N-terminal fragment of pro–(B-type) natriuretic peptide (NT-proBNP) at rest versus electrocardiographic exercise test in stable angina patients without left ventricular dysfunction. *PhD Dissertation*
7. Hill, S. A., Booth, R. A., Santaguida, P. L., Don-Wauchope, A., Brown, J. A., Oremus, M., Ali, U., Bustamam, A., Sohel, N., McKelvie, R., Balion, C. and Raina, P. (2014) Use of BNP and NT-proBNP for the diagnosis of heart failure in the emergency department: A systematic review of the evidence. *Heart Fail. Rev*. 19, 421-438.
8. Zhang, Z. L., Li, R., Yang, F. Y. and Xi, L. (2018) Natriuretic peptide family as diagnostic/prognostic biomarker and treatment modality in management of adult and geriatric patients with heart failure: remaining issues and challenges. *J. Geriatr. Cardiol*. 15, 540-546.

9. Fuery, M. A., Leifer, E. S., Samsky, M. D., Sen, S., O'Connor, C. M., Fiuzat, M., Ezekowitz J., Piña I., Whellan D., , D., Felker G. M., Desai N. R., Januzzi J. L. and Ahmad, T. (2024) Prognostic impact of repeated NT-proBNP measurements in patients with heart failure with reduced ejection fraction. *Heart Fail*. 12, 479-487.

10. Myhre, P. L., Claggett, B., Ballantyne, C. M., Hoogeveen, R. C., Selvin, E., Matsushita, K., Kitzman, D., Konety S., Mosley T. and Shah A. M. (2024)NT-proBNP and Cardiac Troponin I, but Not Cardiac Troponin T, Are Associated With 7-Year Changes in Cardiac Structure and Function in Older Adults: The ARIC Study. *Circulation*.150, 1847-1857.

11. Jhund, P. S., Anand, I. S., Komajda, M., Claggett, B. L., McKelvie, R. S., Zile, M. R., Carson, P. E., McMurray, J. J. V. (2015) Changes in N-terminal pro-B-type natriuretic peptide levels and outcomes in heart failure with preserved ejection fraction: an analysis of the I-Preserve study. *Eur. J. Heart Fail*.17, 809-817.

12. Jones, N. R., Taylor, K. S., Ordóñez-Mena, J. M., Goyder, C. R., Hobbs, F. D. R. and Taylor, C. J.. (2025) NT-proBNP testing for heart failure diagnosis in people with atrial fibrillation: A diagnostic accuracy study. *PLoS Med*.22, e1004550.

13. Myhre, P. L., Vaduganathan, M., Claggett, B. L., Miao Z. M., Jhund, P. S., de Boer, R. A., *et al*. (2022) Influence of NT-proBNP on efficacy of dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *JAAC Heart Fail*. 10, 902-913.

14. Troughton, R., Felker, G. M. and Januzzi Jr, J. L. (2014) Natriuretic peptide-guided heart failure management. *Eur. Heart J*. 35, 16-24.

15. Mair, J., Hammerer-Lercher, A. and Puschendorf, B. (2001) The impact of cardiac natriuretic peptide determination on the diagnosis and management of heart failure. *Clin. Chem. Lab. Med*. 39, 671-588.

16. Bianca-Ștefania, P., Lupașcu, F. G., Stătescu, C., Șorodoc, V., Radu-Andy S., Profire, L. and Șorodoc, L. (2025) Heart Failure Biomarkers—Pathophysiology, Diagnosis, Prognosis and Clinical Relevance. *Int. J. Mol. Sci*. 26, 9740-9771.

17. Felker, G. M., Anstrom, K. J., Adams, K. F., Ezekowitz, J. A., Fiuzat, M., Houston-Miller, N., *et al*. (2017) Effect of Natriuretic Peptide-Guided Therapy on Hospitalization or Cardiovascular Mortality in High-Risk Patients With Heart Failure and Reduced Ejection Fraction: A Randomized Clinical Trial. *JAMA*. 318, 713-720.

18. Misra, A. and Khurana, L.(2011) Obesity-related non-communicable diseases: South Asians vs White Caucasians. *Int. J. Obes*. 35, 167-187.

19. McDonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., Böhm, M., Burri H., Butler J. *et al* (2023) Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur. Heart J*. 44, 3627-3639.

Corresponding Author

Junaid Mahmood Alam
Department of Clinical Biochemistry lab services and
Chemical Pathology, LNH and Medical College,
Karachi-Pakistan
E.mail: drjma1965@yahoo.com